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Chapter 2

Citrus: An Ancient Fruits of Promise for Health Benefits

Waseem Ahmed and Rafia Azmat

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Abstract

Citrus is a group of fruit species, comprise an impressive list of additional vital nutrients, quite heterogeneous in many aspects and ancient times used to prevent and cure different diseases of the human body. It has a range of bioactive chemicals which is suitable for balanced diet and health. Citrus is one of the most important fruit in the world for health-related elements. Some species of the citrus act as a source of potential antioxidant showed prevention against heart diseases, anticancer, inflammation, antiviral, antibacterial and antifungal activity. Citrus fruit contained a higher level of flavonoids, terpenes, phytonutrients and range of phenolic compounds, vitamins C and carotenoids. These biochemicals are present in fruit rag, juice, seed and peel. The biocompounds present in citrus depend upon production, species to species. The aims and objectives of this chapter are to highlight the primary bioactive compounds in citrus and their role in controlling of diseases of a human.

Keywords: grapefruit, health related elements, bioactive compounds

1. Introduction

Citrus fruits are outstanding immune-enhancing source of vitamin C, belong to the family of Rutaceae, grown worldwide, including the members of Sweet oranges, Mandarins, Limes, Grapefruits, Lemons, and Citrons, etc. in which sweet oranges contribute almost 70% [1, 2]. Citrus fruits, being a perennial and tropical crop, subjected to significant seasonal variations of the climate changes during its growth and maturity periods [1]. Citrus fruits cultivated in more than 64 countries throughout the world [2] where annual production reaches 105.4 million tons among the fruit crops [3]. The main fruits crop in Pakistan is citrus which covers a prevalent area of cultivation [4] and acquired 12th position all over the world in citrus production with a landmark of 199,000 acres followed by overall yearly production of 2.36

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million tonnes [2]. There four and five group of citrus fruits which include grapefruit, pummelo, sweet oranges, lemons and mandarins [3]. These citrus fruits are the precious resource of phytochemicals which are beneficial for the human body as vital bioactive medicines [5]. The last two to three decades, there has been a growing consciousness of diet and irrelevant diet causing different diseases in the human body [3]. Depending on the geographical area, growing season and harvesting time, these environmental conditions could be more or less limiting factors for bioactive compounds synthesis, accumulation, and formation [5]. Research programs initiated to improve the quality of citrus fruit with sound management practices [4, 5]. However, there appear to be slightly limited data available on the seasonal accumulation of bioactive compounds during their growing seasons [6]. Citrus has a unique value of essential nutrients, and these nutrients protect against several chronic diseases of the human body [5, 6]. It is utmost significant fruitlet of the biosphere after grapes and has marvelous economic, social and cultural impact on the society [4]. Bioactive compounds are the higher class of secondary plant metabolites which contained 9000 structures but popular and famous in citrus juice and its parts (rag, peel, seeds) [7]. Flavonoids and phenolic compounds derived from 2-phenylchromane commonly found in many vegetables, fruits, and especially citrus possess flavonoids, polyphenols, and antioxidants in a massive amount in different parts such as a peel, rags, juices and seeds [8]. Citrus has potential health benefits like antimicrobial, anti-inflammatory, antiviral and anticancer [9]. The world trend emphasis in natural bioactive compounds in plants and these compounds remain well known for their essential role in human health [10]. The maturity had a relationship with these bioactive compounds, and immature and early harvested fruits showed lower concentrations of these essential compounds [10, 11]. Maturity is a critical factor for responsible of its quality changes during growth and developmental stages of citrus health and full mature fruit was harvested [8, 9]. The abiotic stress involve the effect of the various quality parameters of citrus fruits [9, 10]. Citrus juice contains a lower amount of cholesterol that helps for diabetes patients [11]. Recently, the physical and chemical changes of pomegranate fruit have reported which showed that composition of minerals vary markedly among the three ripening stages [10]. The effects of maturity stages on change of bioactive compounds of berries were reported in [9].

2. Nature and occurrence of phytochemicals in citrus

Phytochemicals are naturally present in citrus juices, grouped into diverse chemicals and play a role in physiological functions and metabolic change of human body [18]. It comprises different phenolic compounds including the saponins, sulfides, phytosterols, carotenoids, monoterpenes, and inhibitors protease [10]. Phytochemicals play a vital role in mediating the plants against environmental stress through proactive compounds. These compounds act as signaling fascinating molecules provide protection and resistance against pathogenic diseases. In citrus, a wide range of phytochemicals and its distribution reported in its various parts [8]. These chemicals are helpful in different oxidative stress involved in the balanced and coordinate system to improve the human body. They have linked with a different range of enzymes and created a signal pathway with different organs and maintained the human metabolites [10, 11].

2.1. Citrus nutritional functioning of phytochemicals

Fruit and vegetables are the best natural resource of phytochemicals which play a vital function in the prevention of infectious diseases [12]. These phytochemicals disclose the promising health effects in acting as antioxidants, controlling blood sugar and blood pressure [5]. Citrus phytochemicals also exhibit the antibacterial, antiviral, antifungal, anti-carcinogenic, antithrombotic or anti-inflammatory properties followed by cholesterol-lowering assets [11]. These active compounds are phenols, carotenoids, phytoestrogen and sulfides having antioxidative potential, and marked as health promotor due to their broad spectrum in the human body [10–12]. The purpose of perspective and analysis of extraction of essential compounds of citrus as presented in **Figure 1**.

2.2. Citrus phytochemical classes and its distribution in various parts

2.2.1. Flavonoids

Flavonoids are leading miscellaneous assembly of phytonutrients to present virtually almost in all fruits and vegetable with more than 6000 types [13]. The flavonoids basic structure of comprises of a frame of diphenyl propane, having two aromatic benzene (ring A and B) allied through a three carbon chain which forms a closed pyran ring using benzene A ring [15]. Consequently, their structure is also denoted as C_6-C_3-C_6 [16]. They are classified as flavanones, flavones, and flavonols, in which more than 60 individual flavonoids identifies in citrus now [14]. They are present in the form of the glycoside or aglycone, especially in citrus juices as glycosyl derivatives (flavonoid glycosides, FGs) which showed potential health benefits for human body [3]. Glycoside forms consist of two types of di-glycosides, L-rhamnosyl-glucosyl derivatives, which are classified as neohesperidosides and rutinosides, connected through 1,2 or 1,6 inter glycosidic bond, respectively. It had excellent potential to control

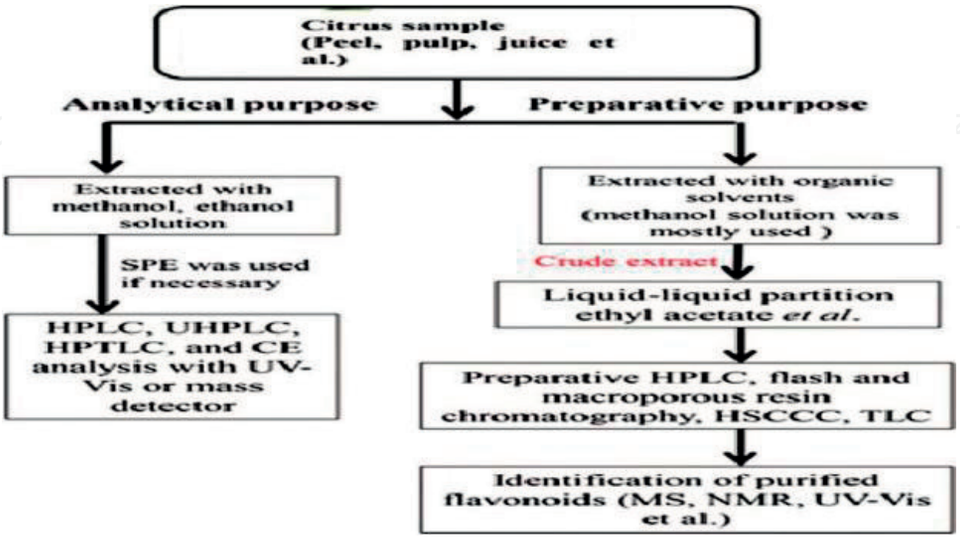

Figure 1. The schematic flow of analytical techniques for isolation of health-related elements.

many chronic diseases and suppressed the infectious in the body [13, 14]. The classification of flavonoids showed in **Figure 2**. The exaction methods and bioactivity of significant citrus compounds are shown in **Figure 3**.

2.2.2. Glucosinolates

The significant phytochemicals group is sulfur compounds which are present in higher quantity in seeds and peel of citrus, converted into isothiocyanates and showed properties of anti-infective followed to improve mucus. They also help in cancer control in the human body [14, 15].

2.2.3. Essential oil

Mostly citrus species have a rich source of aromatic compounds; have more than 400 compounds with volatile and nonvolatile compounds [16, 17]. Citrus peel is a rich source of essential oil and used as more than thousands of medicine, these compounds used in various cosmetics, the pharmacy-related industry. Moreover, 10 kg of citrus peel produced an essential oil of 1 ml, showed the properties of antispasmodic and antimicrobial activity [14].

2.3. Mucilage

Mucilage is present in seed, peel and rag of citrus species; it is a fiber-like and forms a gel-like structure which mixed with water [17]. The seeds of citrus have psyllium, with improving the digestives system, improving the functioning of the intestines and facilitating the elimination of cholesterol [18].

2.3.1. Tannins

The grapefruit, lemon and lime are rich source of tannins compounds, they also have the ability to stop diarrhea and reduce bleeding and controls other excessive secretions of body [19].

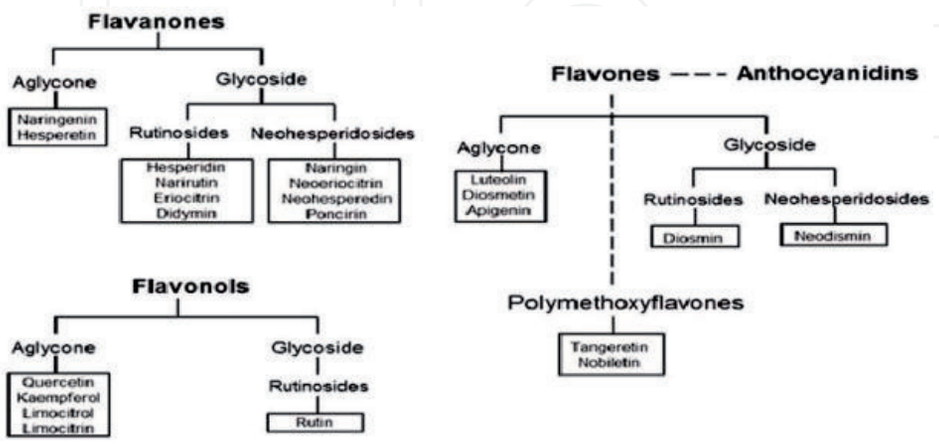

Figure 2. The major classification of health-related elements in citrus.

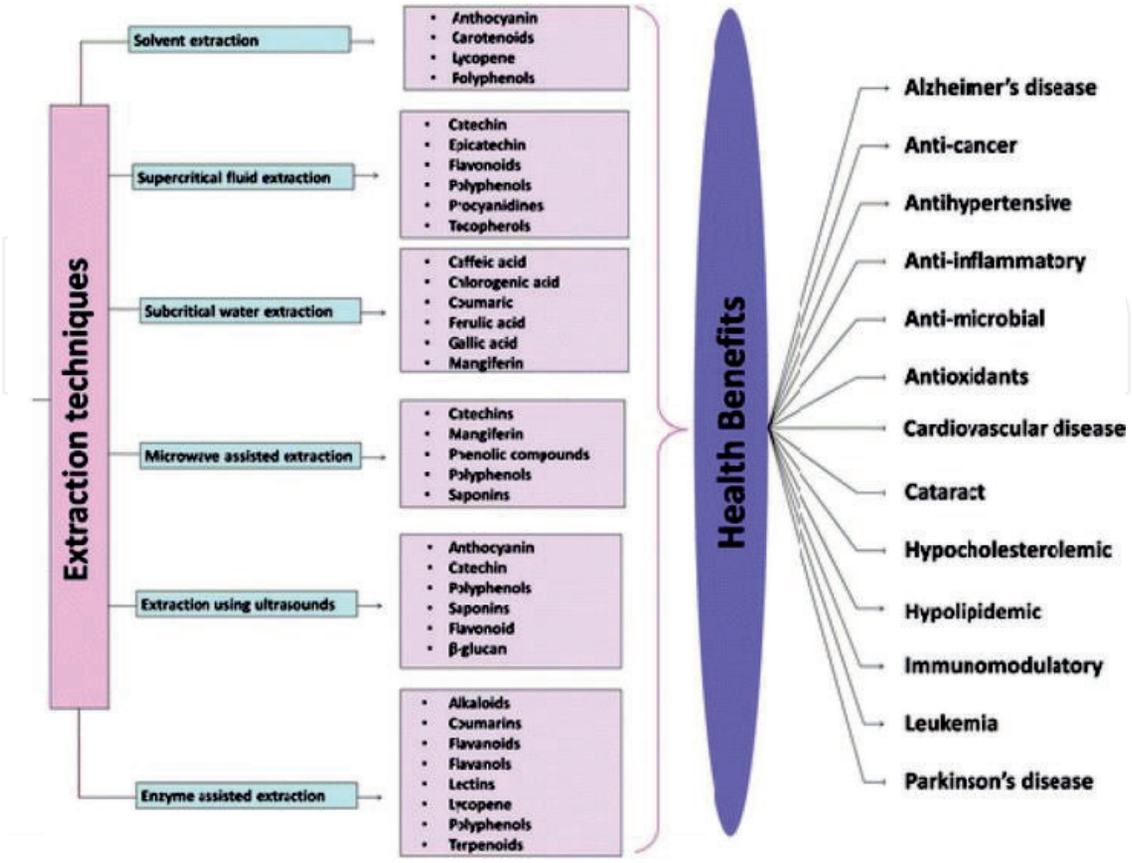

Figure 3. Various extraction methods of bioactive compounds in citrus and their impact on health.

2.4. Role of phytonutrients in the human body

Naturally, the citrus pulp comprised of 85–90% water and more than 300 compounds [13]. The composition of citrus fruits varies with the nature of species, cultivar, agro-climatic conditions, cultivation practices and rootstocks [12]. The role of citrus bioactive compounds is ancient and traditionally used in the early twentieth century [13]. The citrus flavonoids were found to help in capillary fragility. A detailed literature search indicates a positive correlation between consumption of citrus fruits and reduced incidence of ischemic stroke [14]. Flavonoids, terpenoids, carotenoids, and coumarins as primary and, secondary metabolites accumulated in edible as well as inedible parts of citrus fruit tissues [14]. Monoterpenes are the principal components of essential oil and contribute to aroma and flavor of citrus. Many of these monoterpenes are believed to exhibit health beneficial properties owing to their antioxidant and anti-cancer activities [20]. However, the recent enthusiasm about health beneficial properties of citrus centered on the flavonoids and the limonoids. The dietary fiber, carotenoids, saponins, protease, indole, and isoflavones are found in the citrus fruit. While the juice of citrus categorized through their distinctive odor, attractive perception and accepted as an essential diet and act as an essential part of natural nutrition, display central characters in providing energy and nutrients for health advancement. Citrus well recognized due to its low protein and fats, supply sucrose, glucose, and fructose in the form of carbohydrates [13].

Citrus is a good resource of nutritional integrity, which linked with lowering cholesterol and prevention of gastrointestinal diseases. Citrus juice is the excellent resource of Vitamin C followed by B vitamins including thiamin, pyridoxine, niacin, riboflavin, pantothenic acid, and folate [15]. The citrus fruits help in reducing the risk of many chronic diseases through significant phytochemicals like carotenoids, flavonoids, and limonoids [21].

2.5. Citrus phytonutrient role in the human body

The citrus fruit contained a massive amount of minerals and vitamins. In sweet oranges, the range of phytonutrients more as compares to limes, similar to the higher range of phytonutrient found in grapefruit and lemons. The naturally occurring folate and water-soluble vitamins in citrus can act as a coenzyme and involve in many biological process methylation, repair of DNA cell division growth and development of new cells. Usually, citrus is consumed in the form of the fresh juice while the vital phytonutrients showed in **Table 1**.

2.6. The major carotenoids in citrus fruits

The primary role of carotenoids pigment compounds to protect the various diseases of the human body and control-health-related elements; sweet orange, mandarin's and grapefruits are a rich source of carotenoids. Lutein and zeaxanthin are rich sources of citrus which are suitable for eyes and immunes system of the body. A vibrant source of carotenoids present in

Sr. no	Minerals	Health promoting elements in citrus
1	Copper	Copper is trace element for essential in health
2.	Calcium	It is main part in bones, teeth and major role in metabolism
3.	Manganese	It involves in metal enzymatic activity and fat metabolism
4.	Magnesium	Muscles contraction
5.	Selenium	Antioxidants role in body process
6.	Potassium	Role in fluid system and assists in nervous system
7.	Phosphorus	It is involves in DNA and part of energy distributions
8.	Sodium	Its balance the human body and nerves and muscles functions
9.	Zinc	Blood circulation and metabolism in body
10.	Vitamin B1 (thiamin)	Heart, brain, nervous system, cofactor in gastrointestinal, muscular functions
11.	Vitamin B2 (riboflavin)	Reduction reactions and coenzyme in oxidation
12.	Vitamin B3 (niacin)	System metabolism, maintained circuitry system
13.	Vitamin B6 (piridoxina)	Its balance the body, fluid, metabolism, hemoglobin
14.	Vitamin B9 (folic acid)	It play a role in an acid, nucleic acid and metabolism balance
15	Vitamin C (ascorbic acid)	Formation of connective tissues, collagen, absorption of iron and properties of antioxidants

Table 1. General table of phytonutrients in citrus.

Cara navel oranges and mandarin fruits. The comparison of significant carotenoids present in citrus fruits shown in **Table 2**.

2.7. Flavonoids (flavones, flavonols and flavanols or catechins)

Flavonoids are polyphenol compounds that occur in plant-based food, more than 400 flavonoids have been indefinite in fruit and vegetables, but the significant flavonoid sources are citrus fruits [14, 15]. Flavonoids are usually present as glycosides; Citrus juice showed mostly biological activity whereas its antioxidants potential activity is more important. The activity based on tumor control, heart diseases, daily intake of flavonoids is a significant balance of disease in the human body [13]. The citrus considered as affluent fruit springs for sinensetin (peel oils and juice), total polymethoxylated flavones (mandarins and oranges peel oils), and tangeretins Limes juice has been used to control cholera which contains luteolin and tangeretin. The comparison of different flavonoids found in citrus species shown in **Table 3**.

2.8. Phytosterols in citrus

The citrus sterols used in different medicine while citrus juice has permanently linked to cancer prevention and reduction of cholesterol. The significant phytosterols present in grapefruit and oranges, and are helpful in stomach cancer, colon, rectal. The phytosterols are also involved in weight loss. The citrus peel is a precious resource of volatile compounds with a range of 95–98%. The significant phytosterols present in different citrus species shown in **Table 4**.

2.9. Role of phytochemicals of citrus in different diseases of the human body

2.9.1. Cancer

The scientific community engaged in the role of citrus flavonoids, phenolic compounds in the prevention of cancer disease and its use in the drug. Mostly cancer is caused by improper

Citrus species						
Carotenoids mg/110 g	**Grapefruit**	**Oranges**	**Lemon**	**Oranges valencia**	**Tangerine**	**Mandarin**
Auroxanthin	—	0.23	—	—	—	—
Cis β-carotene	—	—	—	—	—	11
α-Carotene	1	19–20		—	1	12–20
Cryptoxanthin	3.3	—	—	—	—	10-20
β-Cryptoxanthin	150	—	—	—	—	—
α-Cryptoxanthin	Present	—	—	—	—	—
Lutein	9.5	27		20–35	106	20–50
Luteoxan	Present	—	—	—	—	—
Lycopene	1	—	—	3–4	—	—

Table 2. Major group of carotenoids found in citrus.

Flavonoids ug/110 g	Grapefruit	Oranges	Lemon	Oranges valencia	Tangerine	Mandarin
Apigenin	—	—	—	0–0.3	—	—
Acacetin	—	—	—	—	—	—
Hexamethoflavone	—	—	—	0.3	—	—
Polymethoxylated flavones	—	0.2	—	—	—	0.65–0.72
Myricetin	—	0.0–0.05	—	—	0.1	—
Quercetin	0.49–0.70	0.57	—	—	—	—
Sinensetin	—	—	—	—	—	20–70
Tangeretin	0–120	—	—	—	190	0–180
Violaxanthin	—	—	—		—	12

Table 3. Major group of flavonoids found in citrus.

Phytosterols ug/110 g	Grapefruit	Oranges	Lemon	Oranges valencia	Tangerine	Mandarin
Auraptene	0.14–0.17	0.13	—	—	—	—
Coumarin	0.26	0.54	—	—	—	—
Meranzin	0.16–0.25	0.55	—	—	—	—

Table 4. Phytosterols in citrus distribution.

diet intake [6]. The colon cancer is a serious issue caused by the imbalances and wrong uses of diet. Mostly 90% cases of colon cancer have reported in the world due to diet. The tyrosine modulator as citrus flavonoids is useful in cancer treatments. Several studies reported that in treatments of different cancers lines the juice of citrus showed an antiproliferative. The role of flavonoids (nobiletin, hesperetin, tangeretin and neohesperetin) is tumor controlling activity in the human body. The citrus peel oil like d-limonene showed an anticancerous activity, especially peel oil of citrus effective in skin cancer control. It is like a sheet in the tumor cell, and oil application suppresses mostly cell [15].

2.9.2. Oxidative damage, cardiovascular and coronary heart diseases (CVD and CHD)

The cardiovascular diseases stand as real problems of this world with many deaths has been reported yearly while the drug resistance is more prominent in the world. The save and sound methods required for the isolation of citrus new bioactive compounds in juice, peel rag, and seeds. This area of investigation required more attention of the scientists for the development of new natural methods of isolation of active compounds from citrus fruits like lemons, grapefruits, sweet oranges, involves in treatments of hypertension. The chronic, hemorrhoids and leg cancer, the 6, 8-di-*C*-glucosyldiosmetin and Vicenin-2 suppressive of blood adhesion molecules are mostly found in citrus. The different citrus extracts were significant control of

hemorrhages. The principal role of flavonoids chrysin, luteolin, 7-hydroxyflavone on induced on the umbilical vein, the lipoprotein. The body of human cell endothelial cells oxidized LDL and stimulated the more intracellular production of ROS. These bioactive compounds managed under the control of LDL. The bioactive compounds are better for hypercholesterolemia and atherosclerosis control.

2.9.3. Role of citrus juice on lipid metabolism and obesity control

Polyphenols from citrus fruits have been evaluated in prevention and treatment of obesity. The role of nobiletin, flavones, and hesperidin in hepatic mechanisms are extraordinary. The lemon and sweet orange have a vast range of bioactive compounds with reported a 60–70% control of liver diseases [13]. The grapefruit juices have individual enzymes which control the obesity of human body. The adipose tissue has a significant role in energy storage, but it performed several functions in human tissues to joined with endocrine organ due to paracrine secreted called adipokines [15]. The tissues involved in the signal pathway of endocrine glands. The grapefruit juice contained enzymes called P-45 and range of different protein which burn human fats [14]. The lemon has many bioactive compounds, and the juice of lemon possesses more than 200 compounds which involve regulators of the human body [14]. Many clinical studies approve the citrus juice is beneficial for control higher cholesterol and major lipid problem of the human body [6, 7]. In a world mostly death has been reported by the obesity while the health drinks with full of nutrients shown significant role in the reduction of fats in the human body [17].

2.9.4. Anti-microbial activity

Citrus fruit is a rich resource of flavonoids with many physiological properties involved in controlling antiviral activity and anti-microbial activity. Hesperidin and quercetin involve in control of herpes virus, parainfluenza and polioviruses [15]. The naringin metabolites are rich source of natural antimicrobials activity against the positive and negative bacteria [4]. The sweet oranges and grapefruit is a rich source of phytochemicals, suitable for microbial control.

2.9.5. Role of citrus nutrigenomics

The dietary phytochemicals showed a gene expression in many processes of the human body. The gene and nutritional approaches have linked with health. The bioactive compounds can normalize the transcriptome gene expression. The different studies have shown that activation of gene and modulating the targeted molecules. The study showed a lower density lipoprotein receptor expression by citrus flavonoids. The citrus flavonoids and carotenoids showed a different genes expression COX-2, NFkB and cytochrome P450. The citrus fruits have a range of biological activity for maintaining the health of different organs [22, 23].

2.9.6. Activity against other diseases

Citrus has a precious resource of soluble and insoluble fiber with several benefits in preserving and removal of toxic effects in the body [13]. Fiber improves the gastric adsorption in the

small intestine like the gastric emptying, reduces the energy absorption process, the bile duct and liver maintaining [14]. Fiber and pectin of citrus in the small intestine of human recover the weight of villus and depth of crypt depth [15]. Cell proliferation of an intestinal cell, brush border membrane enzymes and the short-chain fatty acid production in the cecum stimulated by pectin are followed by an increase in the plasma level. It is also a factor for the illegal growth of mucosal. In the gastric tract, the cell promotes the efficiency of the track. All these changes are closely related to the modification of proteins with energy linked [15, 16].

3. Conclusions

Citrus is a significant source of bioactive compounds; the bioactive compounds are suitable for controlling different human diseases. The bioactive compounds have saved and healthy effects on diseases. The Citrus fruits and their components have a rich source of flavonoids, carotenoids, and bioactive compounds. There is a need for the development of awareness and uses of such compounds in life for saving the life threating diseases by using the bioactive compounds. The world always focused on the proper uses and consumption of citrus fruits and juices in our daily life. This chapter discloses the important compounds found in citrus that are highly required by the human body and their use play a significant impact on the human life for diseases controls.

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Conflict of interest

The author of this chapter declares that there is no conflict of interest among the author of this project.

Author details

Waseem Ahmed[1]* and Rafia Azmat[2]

*Address all correspondence to: waseemuaf12@gmail.com

1 Department of Horticulture, University of Haripur, Pakistan

2 Department of Chemistry, University of Karachi, Pakistan

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